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07/762,762	09/16/91	THOMPSON	CGNE-69-4

EXAMINER	
MOODY, P	
ART UNIT	**PAPER NUMBER**
1804	20

18M2/0921

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DATE MAILED: 09/21/93

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 24 June 1993 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire THREE (3) month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449. 1 of 1
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 18-26, 33-36, 38-41, 68-82 are pending in the application.
   Of the above, claims 19-20, 23-25, 34, 38-40 are withdrawn from consideration.
2. ☒ Claims 1-17, 27-32, 37, 42-67 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 18, 21-22, 26, 33, 35-36, 41, 68-82 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Analyses of transformed plants disclosed at pages 110-114 of this specification and Figure 5 (jojoba desaturase) are not found in any prior application. Subject matter found in Figures 3, 4A-4C, 7B-C, and portions of Figure 8 are found in only one parent application, S.N. 07/615784 (filed 14 November 1990). All other subject matter appears to benefit at least from the earliest filing date of S.N. 07/494106 (filed 16 March 1990).

Amendments to page 11, line 23 and page 40, line 26 have not been entered as the indicated words could not be found at that location.

The amendment filed 24 June 1993 is objected to under 35 U.S.C. § 132 because it introduces new matter into the specification. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: Page 9, line 23 adding Figure 11 brief description and instruction at page 4 of the response to add the enclosed Figure 11.

Applicant is required to cancel the new matter in the response to this Office action.

Claims 19-20, 23-25, 34, and 38-40 stand withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected species and subspecies, the requirement having been traversed in Paper No. 15. The species and subspecies of the process claims are unrelated and have different properties as claimed and are capable of separate manufacture and use and are patentably distinct as noted in the

last office action and will not be examined upon indication of allowable subject matter. Applicant has not submitted evidence for the record or clearly admitted on the record that these are obvious variants.

Portions of the information disclosure statement filed 24 June 1993 were not considered because some entries are redundant in this record and because it is improper to cite references found in later filed applications. It is also improper to recite related applications on an equivalent 1449 form; this information can be supplied by means of an information disclosure statement.

The rejection of claim 35 under 35 U.S.C. § 112, second paragraph, is withdrawn in view of applicants remarks filed 24 June 1993.

Claims 18, 21-22, 26, 33, 35-36, and 41 remain (claim 37 now cancelled) and new claims 68-82 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18, 21-22, and 26 appear to be substantial duplicates of claims 33, 36 and 41. Likewise, claims 68-72 appear to substantially duplicate claims 76-79; and claims 73-75 appear to substantially duplicate claims 80-82. All other portions of this rejection are withdrawn in view of cancelled and amended claims and the response filed 24 June 1993.

Applicant's arguments filed 24 June 1993 have been fully considered but they are not deemed to be persuasive. Remarks

concerning distinctions between fatty acid pools and fatty acids in the form of a triglyceride in relation to the restriction requirement are not correct. The restriction requirement made no such distinction and Applicant's position with respect to the claims is inconsistent because the remarks appear to lead to a conclusion that one set of claims is not drawn to the elected invention. If applicant wishes to describe the measured fatty acid composition as being fatty acids or, alternatively, as being triglycerides, applicant may do so even though this seems unnecessarily redundant and the specification makes no note of distinction in the use of these terms; however, dependent claims 22 and 72 would still be redundant over claims 33 and 76.

New claims 74, 79, and 81 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 79 fails to further limit the invention of claim 76. Claims 74 and 81 are vague and indefinite and unclear for "homologous" -- is the cloned sequence derived from the host cell?

Claims 18, 21-22, 26, 33, 35-36, and 41 remain rejected (claim 37 now cancelled) and new claims 68-82 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention.

The portion of this rejection dealing with "modifying portion of" a desaturase is withdrawn in view of amended claims.

The content of the constructs used in the disclosed process at pages 110-114 is unclear because the written description is difficult to follow and there are no drawings of the constructs. For example, pCGN3242 (discussed at pages 106-107) either has two copies of antisense desaturase (of undetermined length and composition) under the control of two different promoters--or one copy controlled by an inserted napin promoter and it is unclear what happened to the "ACP" promoter. The pCGN3234 construct is less confusing only in the sense that at least one antisense oriented desaturase cDNA (undetermine origin and length) is under the control of a CaMV35S promoter (page 110); however, the disclosure teaches that this does not work well and is clearly not the preferred best mode. For these reasons, the Examiner cannot determine what is necessary to acheive the stated end result. The claims are incomplete for failing to recite elements necessary to acheive the stated end result such as some type of antisense orientation for desaturase cDNA; but it is not clear what portion(s) must be in the antisense orientation or what other elements must be included in the claimed process in order to acheive the stated result based on the disclosure as filed.

Applicant's arguments filed 24 June 1993 have been fully considered but they are not deemed to be persuasive. Figure 11 supplied with the response was considered to the extent that it represents an exhibit in rebuttal. Figure 11 shows two plasmids having one antisense construct with a different promoter in each plasmid and a third plasmid containing both of these constructs. This is not found in the disclosure and is new matter as noted above. Remarks in the response cannot correct deficiencies in the specification as filed. It is not clear what applicant was using to obtain modifications and thus it is not clear what, if anything, was needed to describe the invention.

The specification remains objected to under 35 U.S.C. § 112, first paragraph as failing to provide a full written description and enablement for practicing the claimed invention as stated in the last office action and repeated herein.

The process of modifying oil composition of Brassica by transformation with antisense oriented stearoyl-ACP (a.k.a. Δ9) desaturase cDNA from Brassica under the control of seed-specific promoters (pages 110-113) does not apparently produce all sorts of modifications but rather only appears to increase stearic acid in some but not all progeny and apparently in a continuously variable range of from 22.9% up to 45% in the two Brassica species tested. The composition of the construct used, pCGN3242, (see pages 106-107) is unclear as noted above; and it is unclear whether other plasmids could be constructed which would function similarly and thus obviate a need for a deposit. The process clearly requires choice of the proper construct for success (e.g., choice of promoter) but those features which are peculiar to this plasmid or which are general features that could be constructed in any plasmid are unclear. Since it is not clear what the content of this plasmid is, the Examiner takes the position that this plasmid is essential to the invention in the absence of clear and convincing evidence to the contrary.

Since pCGN3242 (used in the example at pages 110-113) is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If not so obtainable or available, the requirements of 35 USC 112 may be satisfied by a deposit of the plasmid in a recognized utility patent depository. The specification does not disclose a repeatable process to obtain the plasmid and it is not apparent if it is readily available to the public. Therefore, a deposit of plasmid is required. See 37 CFR 1.802.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. See CFR 1.808.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801 - 37 CFR 1.809, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and
(e) the deposit will be replaced if it should ever become inviable.

In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

Claims 18, 21-22, 26, 33, 35-36, and 41 remain (claim 37 now cancelled) and new claims 68-82 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Applicant's arguments filed 24 June 1993 have been fully considered but they are not deemed to be persuasive. Arguments from page 20-22 of the response suggest an invitation to experiment. As noted above Figure 11 is deemed to be new matter as the description in the specification as filed does not clearly convey the information found in Figure 11 and remarks in the response cannot cure defects in the specification as filed.

Claims 18, 21-22, 26, 33, 35-36, and 41 remain (claim 37 now cancelled) and new claims 68-69, 71-74, 76-77, and 79-81 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to a process of modifying oil composition of Brassica by transformation with antisense oriented stearoyl-ACP (a.k.a. Δ9) desaturase cDNA from Brassica under the control of seed-specific promoters as described at pages 110-114. The process does not apparently produce all sorts of modifications but rather only appears to increase stearic acid in some but not all progeny and apparently in a continuously variable range of from 22.9% up to 45% in the two Brassica species tested. See M.P.E.P. §§ 706.03(n) and 706.03(z). No other alteration appears to be reproducible, for example, it is not clear what if anything happens to the oleic

acid (a.k.a. 18:1) fraction which may decrease by about half in some cases (page 110) and remain unchanged in others (top of page 112, it is both decreased and increased). Limitation to specific examples actually disclosed is warranted where unique and unpredictable biochemical and genetic actions are involved. The scope of the claimed invention is not commensurate with the disclosure as filed. See In re Marzocchi, 169 USPQ 367; In re Angstadt and Griffin, 190 USPQ 214; Ex parte Hitzeman, 9 USPQ2d 1821.

Applicant's arguments filed 24 June 1993 have been fully considered but they are not deemed to be persuasive. The efficacy of the Brassica antisense construct in Brassica is not sufficient to warrant extension to efficacy of the construct in any other plant. It is not clear what the Brassica construct contained in terms of sequence, or how that sequence compared among species, and there is no showing that the nucleic acid sequence match among species is sufficient to inhibit message transcription in other species. "Transwitch" is not defined in this specification and no embodiment of this can be found in the disclosure as filed. Expressing an encoded protein is not the same as inhibiting expression by antisense so Example 9 does not appear to be relevant to the issue at hand. Furthermore, it is not clear whether modifications were obtained by expressing the safflower protein of Example 9 and if so, what, if anything, was needed for success. Hoped for results for other types of desaturases active at other points in the biosynthesis pathway (none of which are described in the specification) are not commensurate with the disclosure as filed. The rate-limiting steps are known such that one of skill in the art cannot known what expression parameters to vary and the suggestion to do so is

tantamount to an invitation to experiment. These embodiments provide no guidance or general teaching sufficient to warrant claims which embrace any and all plant desaturases.

Claims 18, 21-22, 26, 33, 35-36, and 41 remain (claim 37 now cancelled) and new claims 68-82 are rejected under 35 U.S.C. § 103 as being unpatentable over Kridl et al (6) taken with Knauf (12) and Shewmaker et al ('065) and further in view of McKeon et al (16) and Weissman et al (3) as applied in the last office action and repeated herein.

The primary reference disclosed all features of the claimed invention including seed specific expression during lipid accumulation by means of napin promoters but differed from the disclosed invention in that the expressed gene was a sense construct of acyl carrier protein rather than an antisense construct of stearoyl-ACP desaturase as in the present invention.

The secondary references disclosed that antisense constructs of fatty acid synthesis pathway genes were a desirable means of altering plant oil composition (Knauf). Shewmaker et al taught that a cDNA sequence was all one of ordinary skill in the art needed in order to make antisense constructs for any plant gene (Shewmaker et al). The tertiary references disclosed purified protein preparations of stearoyl-ACP desaturase from safflower and its role in fatty acid synthesis (McKeon et al) and taught that purified protein preparations were all that one of ordinary skill in the art needed in order to obtain cDNA for any gene (Weissman et al).

At the time this invention was made, it was obvious to one of ordinary skill in the art to modify the primary reference with the teachings of the secondary and tertiary references in order to obtain antisense constructs for any fatty acid pathway enzyme, including stearoyl-ACP desaturase, and down regulate expression of same in plants as suggested by Knauf with a reasonable expectation of success. Thus the invention as claimed was very clearly prima facie obvious as a whole over the prior art in the absence of clear and convincing evidence to the contrary.

Applicant's arguments and the Thompson Declaration filed 24 June 1993 have been fully considered but they are not deemed to be persuasive. The facts in Bell relate to hIGF and the state of the art with respect to hIGF a decade ago. At the time this invention was made it was routine in the art to obtain genes as

applicant himself has done -- that is by sequencing the protein, making a nucleic acid probe optimized for known plant codon preferences, and retrieving the gene from a cloned library as long as a purified preparation was available. The preparation did not even have to be purified to homogeneity as taught by Weissman; note also that in Weissman the need for unique amino acids related to primers not to probes for the gene.

The Kater publication and the untranslated Netherlands patent application appear to have the same nucleic acid sequence (Figure 3 in Kater et al and Figure 1a in the patent starting at +44 -- and presumably not the sequence in this application). One identifies the sequence as 'desaturase' and the other as 'enoyl-ACP reductase'. It is unclear which label is correct or how the different labels came into being but the Kater et al publication (which is in English) indicates that the isolation procedure involved only part of McKeon et al. Different elution conditions were used and the molecular weight of the eluted product was different. This does not appear to relate in any way to the purified protein preparation of stearoyl desaturase by McKeon et al.

The Thompson Declaration says that applicant's preparation obtained by following McKeon et al had 18 kD albumin in it as a minor contaminate but that the 43kD major band was desaturase as taught by McKeon et al. It would appear that the major 43kD band was homogenous. If applicant has any clear and convincing,

sufficient evidence to the contrary, the basis for the rejection may be undermined. The relevance of mole percent is not clear for the record.

Shewmaker generally taught the application of antisense for any gene in order to reduce expression of the message encoding the product of that gene. The disclosed invention appears to be modification with antisense constructs -- the content of which are unclear as noted above -- and these claims offer no specific limitation beyond that taught by Shewmaker i.e. reverse orientation of the coding sequence.

No claim was allowed.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to P. Moody (nee Rhodes) at telephone number (703) 308-0196.

P. Moody
Patent Examiner
Group Art Unit 1804

P. Moody PRM
September 20, 1993